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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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10/527,785

10/03/2005

Marco Cattaruzza

DEBE:053US/10501498

1068

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EXAMINER

WOLLENBERGER, LOUIS V

ART UNIT

PAPER NUMBER

1635

MAIL DATE

DELIVERY MODE

04/03/2009

PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No. 10/527,785	Applicant(s) CATTARUZZA ET AL.	
	Examiner Louis Wollenberger	Art Unit 1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 19 March 2009.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1 and 2 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1 and 2 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Finality of Previous Action Withdrawn

The finality of the previous Office Action is withdrawn in view of the new grounds of rejection set forth below.

Status of Application/Amendment/Claims

Applicant's response filed 3/19/2009 has been considered. Rejections and/or objections not reiterated from the previous office action mailed 1/22/2009 are hereby withdrawn. The following rejections and/or objections are either newly applied or are reiterated and are the only rejections and/or objections presently applied to the instant application. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Applicant's amendment to the claims, filed 3/19/2009, is acknowledged. With entry of the amendment, Claims 1 and 2 are pending and under examination.

Non-Statutory Double Patenting—maintained

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned

with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1 and 2 remain provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 11-19 of copending Application No. 10/526430. Although the conflicting claims are not identical, they are not patentably distinct from each other because conflicting application 10/526430 claims a pharmaceutical formulation comprising a nucleic acid and a nonsteroidal anti-inflammatory drug.

MPEP §804 provides that "...those portions of the specification which provide support for the patent claims may also be examined and considered when addressing the issue of whether a claim in the application defines an obvious variation of an invention claimed in the patent. *In re Vogel*, 422 F.2d 438, 441-42, 164 USPQ 619, 622 (CCPA 1970). The court in *Vogel* recognized "that it is most difficult, if not meaningless, to try to say what is or is not an obvious variation of a claim," but that one can judge whether or not the invention claimed in an application is an obvious variation of an embodiment disclosed in the patent which provides support for the patent claim.

35 USC 112, first paragraph, support for claims 11-19 of copending application 10/526430 finds that the "nucleic acid" recited in the claim may be a decoy oligonucleotide of the type comprising or identical to that now claimed. An updated STIC-Biotech sequence search of instant SEQ ID NO:17 finds that the double stranded oligonucleotides corresponding to SEQ ID Nos. 1, 2, 5, 6, 13, 14, 17, 18, and 37 each comprise instant SEQ ID NO:17. See selected alignments below.

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Thus, given that the "nucleic acid" recited in claims 11-19 of 10/526430 may be any one of the decoy oligonucleotides disclosed in the 10/526430 specification, and given that the instantly claimed decoy is intended for pharmaceutical use to treat an inflammatory condition, such as arthritis, one of ordinary skill in the art would conclude the invention defined in claims 1 and 2 is anticipated by, or would have been an obvious variation of, the invention defined in a claim in the conflicting application.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

```

RESULT 3
US-10-526-430A-17
; Sequence 17, Application US/10526430A
; Publication No. US20060258601A1
; GENERAL INFORMATION:
; APPLICANT: HECKER, MARKUS
; APPLICANT: WAGNER, ADREAS H.
; TITLE OF INVENTION: Functional correction of the -786C/T-variance of the human eNOS-gene
; FILE REFERENCE: DEBE:052US
; CURRENT APPLICATION NUMBER: US/10/526,430A
; CURRENT FILING DATE: 2005-03-01
; PRIOR APPLICATION NUMBER: PCT/DE 03/02901
; PRIOR FILING DATE: 2003-09-12
; PRIOR APPLICATION NUMBER: DE 102 42 319
; PRIOR FILING DATE: 2002-09-12
; NUMBER OF SEQ ID NOS: 63
; SOFTWARE: PatentIn version 3.1
; SEQ ID NO 17
; LENGTH: 16
; TYPE: DNA
; ORGANISM: Artificial Sequence
; FEATURE:
; OTHER INFORMATION: Decoy-Oligonucleotide
US-10-526-430A-17

```

```

Query Match          100.0%; Score 16; DB 14; Length 16;
Best Local Similarity 100.0%; Pred. No. 9e+02;
Matches 16; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

```

```

Qy      1 TCCCTGGCCGGCTGAC 16
          |||||
Db      1 TCCCTGGCCGGCTGAC 16

```

```

RESULT 4
US-10-526-430A-18/c
; Sequence 18, Application US/10526430A
; Publication No. US20060258601A1
; GENERAL INFORMATION:
; APPLICANT: HECKER, MARKUS
; APPLICANT: WAGNER, ADREAS H.
; TITLE OF INVENTION: Functional correction of the -786C/T-variance of the human eNOS-gene
; FILE REFERENCE: DEBE:052US
; CURRENT APPLICATION NUMBER: US/10/526,430A
; CURRENT FILING DATE: 2005-03-01
; PRIOR APPLICATION NUMBER: PCT/DE 03/02901
; PRIOR FILING DATE: 2003-09-12
; PRIOR APPLICATION NUMBER: DE 102 42 319
; PRIOR FILING DATE: 2002-09-12
; NUMBER OF SEQ ID NOS: 63
; SOFTWARE: PatentIn version 3.1
; SEQ ID NO 18
; LENGTH: 16

```

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```
; TYPE: DNA
; ORGANISM: Artificial Sequence
; FEATURE:
; OTHER INFORMATION: Decoy-Oligonucleotide
US-10-526-430A-18
```

```
Query Match          100.0%; Score 16; DB 14; Length 16;
Best Local Similarity 100.0%; Pred. No. 9e+02;
Matches 16; Conservative 0; Mismatches 0; Indels 0; Gaps 0;
```

```
Qy      1 TCCCTGGCCGGCTGAC 16
          |||||
Db      16 TCCCTGGCCGGCTGAC 1
```

```
RESULT 8
US-10-526-430A-13
; Sequence 13, Application US/10526430A
; Publication No. US20060258601A1
; GENERAL INFORMATION:
; APPLICANT: HECKER, MARKUS
; APPLICANT: WAGNER, ADREAS H.
; TITLE OF INVENTION: Functional correction of the -786C/T-variance of the human eNOS-gene
; FILE REFERENCE: DEBE:052US
; CURRENT APPLICATION NUMBER: US/10/526,430A
; CURRENT FILING DATE: 2005-03-01
; PRIOR APPLICATION NUMBER: PCT/DE 03/02901
; PRIOR FILING DATE: 2003-09-12
; PRIOR APPLICATION NUMBER: DE 102 42 319
; PRIOR FILING DATE: 2002-09-12
; NUMBER OF SEQ ID NOS: 63
; SOFTWARE: PatentIn version 3.1
; SEQ ID NO 13
; LENGTH: 19
; TYPE: DNA
; ORGANISM: Artificial Sequence
; FEATURE:
; OTHER INFORMATION: Decoy-Oligonucleotide
US-10-526-430A-13
```

```
Query Match          100.0%; Score 16; DB 14; Length 19;
Best Local Similarity 100.0%; Pred. No. 8.6e+02;
Matches 16; Conservative 0; Mismatches 0; Indels 0; Gaps 0;
```

```
Qy      1 TCCCTGGCCGGCTGAC 16
          |||||
Db      4 TCCCTGGCCGGCTGAC 19
```

```
RESULT 9
US-10-526-430A-14/c
; Sequence 14, Application US/10526430A
; Publication No. US20060258601A1
; GENERAL INFORMATION:
; APPLICANT: HECKER, MARKUS
; APPLICANT: WAGNER, ADREAS H.
; TITLE OF INVENTION: Functional correction of the -786C/T-variance of the human eNOS-gene
; FILE REFERENCE: DEBE:052US
; CURRENT APPLICATION NUMBER: US/10/526,430A
; CURRENT FILING DATE: 2005-03-01
; PRIOR APPLICATION NUMBER: PCT/DE 03/02901
; PRIOR FILING DATE: 2003-09-12
; PRIOR APPLICATION NUMBER: DE 102 42 319
; PRIOR FILING DATE: 2002-09-12
; NUMBER OF SEQ ID NOS: 63
; SOFTWARE: PatentIn version 3.1
; SEQ ID NO 14
; LENGTH: 19
; TYPE: DNA
; ORGANISM: Artificial Sequence
; FEATURE:
; OTHER INFORMATION: Decoy-Oligonucleotide
US-10-526-430A-14
```

```
Query Match          100.0%; Score 16; DB 14; Length 19;
Best Local Similarity 100.0%; Pred. No. 8.6e+02;
Matches 16; Conservative 0; Mismatches 0; Indels 0; Gaps 0;
```

```
Qy      1 TCCCTGGCCGGCTGAC 16
          |||||
Db      16 TCCCTGGCCGGCTGAC 1
```

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```

RESULT 10
US-10-526-430A-37/c
; Sequence 37, Application US/10526430A
; Publication No. US20060258601A1
; GENERAL INFORMATION:
; APPLICANT: HECKER, MARKUS
; APPLICANT: WAGNER, ADREAS H.
; TITLE OF INVENTION: Functional correction of the -786C/T-variance of the human eNOS-gene
; FILE REFERENCE: DEBE:052US
; CURRENT APPLICATION NUMBER: US/10/526,430A
; CURRENT FILING DATE: 2005-03-01
; PRIOR APPLICATION NUMBER: PCT/DE 03/02901
; PRIOR FILING DATE: 2003-09-12
; PRIOR APPLICATION NUMBER: DE 102 42 319
; PRIOR FILING DATE: 2002-09-12
; NUMBER OF SEQ ID NOS: 63
; SOFTWARE: PatentIn version 3.1
; SEQ ID NO 37
; LENGTH: 19
; TYPE: DNA
; ORGANISM: Artificial Sequence
; FEATURE:
; OTHER INFORMATION: DNA Oligonucleotide
US-10-526-430A-37

```

```

Query Match      100.0%; Score 16; DB 14; Length 19;
Best Local Similarity 100.0%; Pred. No. 8.6e+02;
Matches 16; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

```

```

Qy      1 TCCCTGGCCGGCTGAC 16
          |||||
Db      18 TCCCTGGCCGGCTGAC 3

```

Response to Arguments

MPEP 804 states “If a “provisional” nonstatutory obviousness-type double patenting (ODP) rejection is the only rejection remaining in the earlier filed of the two pending applications, while the later-filed application is rejectable on other grounds, the examiner should withdraw that rejection and permit the earlier-filed application to issue as a patent without a terminal disclaimer.”

Further analysis of the U.S. filing dates shows the instant application is the “later-filed application” for purposes of the ODP rejection. See continuing data in each application, and compare the filing dates of PCT/DE03/02901, filed 9/2/2003, with PCT/DE03/03028, filed 9/12/2003. Moreover, the instant ODP rejection is not the only rejection remaining in the instant application and is therefore maintained until such time as the claims no longer conflict or a terminal disclaimer is filed.

Claim Rejections - 35 USC § 103—new

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 1 and 2 are rejected under 35 U.S.C. 103(a) as being unpatentable over Moskowitz (US 2002/0132234) in view of Dzau et al. et al. (WO 95/11687) and Morishita et al. (1997) *Nature Medicine* 3:894-899.

A further search of the prior art with regard to SEQ ID NO:17 finds Moskowitz, which is believed to relevant to the instant claims.

The instant claims embrace double stranded oligonucleotides of up to 30 bp in length, comprising SEQ ID NO:17 and 18.

Moskowitz taught materials and methods for the detection of single nucleotide polymorphisms (SNPs) in the nitric oxide synthase gene. At page 19, paragraph 173, Moskowitz disclosed the C2684T SNP and its relation to the 18-nucleotide DNA binding site of nuclear

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factor 1 (NF1), which is said to consist of 5'-CCCTGGCCGGCTGACCCT-3' (referred to therein as SEQ ID NO:9). As shown by the alignment below. The disclosed binding site (SEQ ID NO:9) comprises nucleotides 2-16 of the 16-nucleotide sequence of instant SEQ ID NO:17. At paragraph 24, the native full-length sequence of the eNOS gene is said to correspond to GenBank AF032908 (SEQ ID NO:1). A review of GenBank AF032908 shows a flanking T nucleotide, 5' to the binding site.

```

RESULT 25
US-09-769-207A-9
; Sequence 9, Application US/09769207A
; Patent No. US20020132234A1
; GENERAL INFORMATION:
; APPLICANT: DsGenes, LLC
; TITLE OF INVENTION: NITRIC OXIDE SYNTHASE GENE DIAGNOSTIC POLYMORPHISMS
; FILE REFERENCE: D2G 2165.1
; CURRENT APPLICATION NUMBER: US/09/769,207A
; CURRENT FILING DATE: 2001-01-24
; PRIOR APPLICATION NUMBER: US 60/177,775
; PRIOR FILING DATE: 2000-01-24
; PRIOR APPLICATION NUMBER: US 60/220,662
; PRIOR FILING DATE: 2000-07-25
; NUMBER OF SEQ ID NOS: 25
; SOFTWARE: PatentIn version 3.0
; SEQ ID NO 9
; LENGTH: 16
; TYPE: DNA
; ORGANISM: Homo sapiens
; FEATURE:
; NAME/KEY: misc_feature
; LOCATION: (1)..(16)
; OTHER INFORMATION: NF1 (nuclear factor 1) binding site/Estrogen receptor binding si
; OTHER INFORMATION: t
US-09-769-207A-9

Query Match          93.8%; Score 15; DB 3; Length 16;
Best Local Similarity 100.0%; Pred. No. 3.1e+03;
Matches 15; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

Qy      2 CCCTGGCCGGCTGAC 16
        |||
Db       1 CCCTGGCCGGCTGAC 15

```

Moskowitz does not disclose double stranded decoy oligonucleotides.

Dzau et al. et al. taught methods and materials for making and using double stranded DNA oligonucleotide decoys to inhibit transcription factor binding for the therapeutic treatment of diseases associated with the binding of endogenous transcription factors. At page 6 it is taught decoys should contain at least about 8 base pairs for sufficient binding and specificity, and that providing the decoys with flanking sequences, ranging from 5 to 50 base pairs, beside the

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binding site enhances binding affinity and/or specificity. In certain embodiments, it is said, the decoys are less than 50 base pairs.

The prior art is replete with disclosures exemplifying the use of double stranded decoys of various sizes with the range recommended by Moskowitz.

For example, Morishita et al. showed the use of a 20-base pair double stranded oligonucleotide decoy, comprising a single NF- κ B binding site and flanking sequences, for inhibiting the binding of nuclear factor- κ B in cells in vivo (page 897 and see entire disclosure).

Therefore the prior art taught the principles for designing and using double stranded oligonucleotide decoys, and specifically exemplified the use of 20-bp double stranded decoys to inhibit transcription factor activity.

Therefore, in view of the prior art teaching that double stranded decoys may be used to inhibit transcription factor activity in cells in vivo, it would have been prima facie obvious to make a double stranded decoy comprising, at a minimum, the NF1 binding site sequence disclosed by Moskowitz et al. to inhibit NF1 activity in cells in vitro and in vivo for research and therapeutic purposes to investigate the relation of transcription factor activity and disease. In view of the statement in Moskowitz et al., disclosing that flanking sequences may enhance binding affinity and specificity, and in view of the disclosure stating these flanking sequences may be 5 to 50 bp in length, and in view of specific exemplary embodiments in the prior art wherein decoys of 20 bp were used effectively to inhibit transcription factor activity in vivo, it would further have been obvious to make decoys to NF1 comprising 5 to 50 flanking base pairs, such as any 20-bp decoy comprising the binding site disclosed by Moskowitz and one or more

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additional nucleotides found in the native sequence (GenBank AF032908). Such decoys would necessarily comprise instant SEQ ID NO:17 and 18 and be expected to have decoy activity.

Amending claim 1 to replace the transitional phrase "comprising" in line 1 with "consisting of" and removing the residual language beginning with the phrase "said double-stranded" in the final two lines of the claim would overcome the instant rejection, as the combination of prior art cited above does not point with sufficient specificity to the 16-bp decoy consisting of SEQ ID NO:17 and 18.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Louis Wollenberger whose telephone number is (571)272-8144. The examiner can normally be reached on M-F, 8 am to 4:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James (Doug) Schultz can be reached on (571)272-0763. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Louis Wollenberger/

Primary Examiner, Art Unit 1635

March 31, 2009